Advanced Regression: 3a Variable selection - Part 2

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What are singularity and multicollinearity?

How to detect singularity and multicollinearity?

- Correlation and covariance matrix
- The rank of a matrix
- Variance inflation factor
- Singular value decomposition and condition number

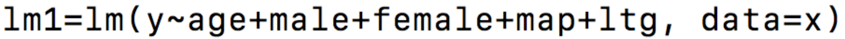
How to prevent multicollinearity?

- Grouping
- Partial least squares
- Pre-whitening

We consider again the diabetes outcome looking at the outcome disease progression y and we try to fit the following linear model

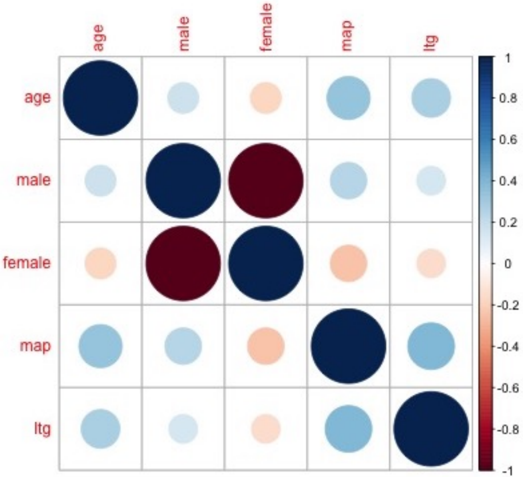
$$y = \alpha + age + male + female + map + ltg$$

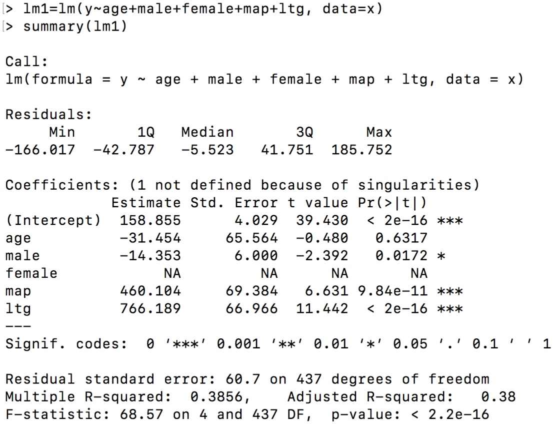
- age: age of the subject
- male: binary indicator if male
- female: binary indicator if female
- map: blood pressure
- ltg: triglycerides



```
lm1=lm(y~age+male+female+map+ltg, data=x)
```

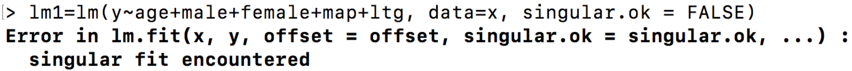
- Visualise the correlation structure using `corrplot()`





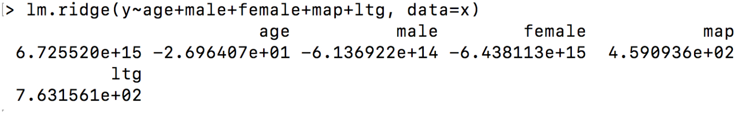
```
> lm1=lm(y~age+male+female+map+ltg, data=x)
> summary(lm1)

Call:
lm(formula = y ~ age + male + female + map + ltg, data = x)

Residuals:
     Min       1Q   Median       3Q      Max 
-166.017  -42.787   -5.523   41.751  185.752 

Coefficients: (1 not defined because of singularities)
            Estimate Std. Error t value Pr(>|t|)    
(Intercept)  158.855      4.029  39.430  < 2e-16 ***
age          -31.454     65.564  -0.480   0.6317    
male         -14.353      6.000  -2.392   0.0172 *  
female            NA         NA      NA       NA    
map          460.104     69.384   6.631 9.84e-11 ***
ltg          766.189     66.966  11.442  < 2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 60.7 on 437 degrees of freedom
Multiple R-squared:  0.3856,    Adjusted R-squared:   0.38 
F-statistic: 68.57 on 4 and 437 DF,  p-value: < 2.2e-16
```

- Option in lm() function: singular.ok = TRUE automatically removes ‘female’.



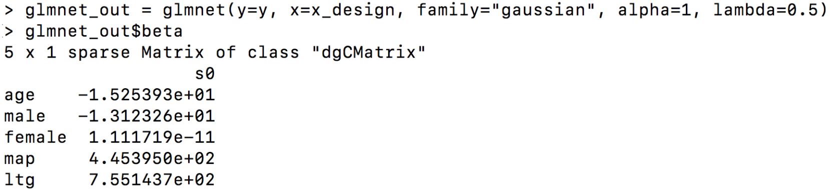
```
> lm1=lm(y~age+male+female+map+ltg, data=x, singular.ok = FALSE)
Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) : 
  singular fit encountered
```

- The lm() function checks for singularities in the design matrix x, but not all methods have this safety check.
- Example: Ridge regression



```
> lm.ridge(y~age+male+female+map+ltg, data=x)
                          age           male         female            map 
 6.725520e+15 -2.696407e+01 -6.136922e+14 -6.438113e+15  4.590936e+02 
          ltg 
 7.631561e+02 
```

- Example: Lasso regression



```
> glmnet_out = glmnet(y=y, x=x_design, family="gaussian", alpha=1, lambda=0.5)
> glmnet_out$beta
5 x 1 sparse Matrix of class "dgCMatrix"
                  s0
age    -1.525393e+01
male   -1.312326e+01
female  1.111719e-11
map     4.453950e+02
ltg     7.551437e+02
```

What are singularity and multicollinearity?

Singularity

One predictor variable in a multiple regression model can be exactly explained by the other $p-1$ predictor variables.

Multicollinearity

One predictor variable in a multiple regression model can be linearly explained by the other $p-1$ predictor variables with high accuracy.

What can cause singularity?

- Dummy-coding of categorical variables. Make sure not to add redundant information.
- Do not include multiple measurements that are measured on different scales (e.g. mol and mmol).

What is the impact of multicollinearity?

True biological processes

do not cause singularity (because they are random, not deterministic), but can cause multicollinearity.

- The computation of the ordinary least squares estimate requires an inversion of the $p \times p$-dimensional correlation matrix $x^t x$.
- $x^t x$ cannot be inverted when the $x^t x$ is singular.
- When there is multicollinearity, $x^t x$ can be inverted, but the estimate will show a high variance and will be highly instable.
- Multicollinearity can distort a linear model and impact the interpretation.

How to inspect correlation structures?

- Correlation and covariance matrix

How to detect singularity?

- Rank of a matrix

How to detect multicollinearity?

- Variance inflation factor
- Condition number based on the ratio of largest over smallest singular value

Covariance matrix

Computing the sample covariance matrix using matrix multiplication

$$\hat{cov}(x) = \frac{1}{n-1} \underbrace{x_c^t}_{p \times n} \underbrace{x_c}_{n \times p}$$

- x_c is centred (mean is zero) $x_c = x - 1_n\bar{x} = cx$
  - where $\bar{x} = (\bar{x}_1, ..., \bar{x}_p)$ is the vector of means
  - and 1_n is a vector of ones
  - and $c = I_n - \frac{1}{n}1_n 1_n^t$
  - and I_n is the $n \times n$ identity matrix with ones on the diagonal
- x predictor matrix of n rows and p columns
- x^t transposed predictor matrix of p rows and n columns

Matrix multiplication

Matrix multiplication: $\underbrace{c}_{n \times p} = \underbrace{a}_{n \times m} \underbrace{b}_{m \times p}$

$$c_{ij} = \sum_{k=1}^{m} a_{ik} b_{kj}$$

- a is a $n \times m$ and b is a $m \times p$ matrix
- c is a $n \times m \times m \times p = n \times p$ matrix
- Make sure your matrices have the correct dimensions, number of columns of the left matrix must be equal to the number of rows on the right.
- Can be computed in R using the $\% * \%$ command.

Correlation matrix

Computing the sample correlation matrix using matrix multiplication

$$\hat{cor}(x) = \frac{1}{n-1} \underbrace{x_s^t}_{p \times n} \underbrace{x_s}_{n \times p}$$

where x_s is a centred and scaled matrix $x_s = cxd^{-1}$

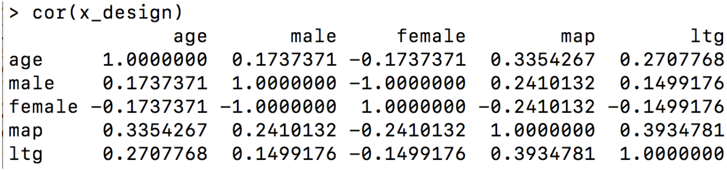
- where $d = diag(s)$ is a diagonal matrix
- with the sample standard deviation s on the diagonal.

This is equivalent to writing

$$\hat{cor}(x_j, x_k) = \frac{\sum_{i=1}^n (x_{ij} - \bar{x}_j)(x_{ik} - \bar{x}_k)}{\sqrt{\sum_{i=1}^n (x_{ij} - \bar{x}_j)^2} \sqrt{\sum_{i=1}^n (x_{ik} - \bar{x}_k)^2}}$$

Correlation matrix

- Correlation matrices are symmetric and have a vector of 1's on the diagonal.



```
> cor(x_design)
              age       male     female        map        ltg
age     1.0000000  0.1737371 -0.1737371  0.3354267  0.2707768
male    0.1737371  1.0000000 -1.0000000  0.2410132  0.1499176
female -0.1737371 -1.0000000  1.0000000 -0.2410132 -0.1499176
map     0.3354267  0.2410132 -0.2410132  1.0000000  0.3934781
ltg     0.2707768  0.1499176 -0.1499176  0.3934781  1.0000000
```

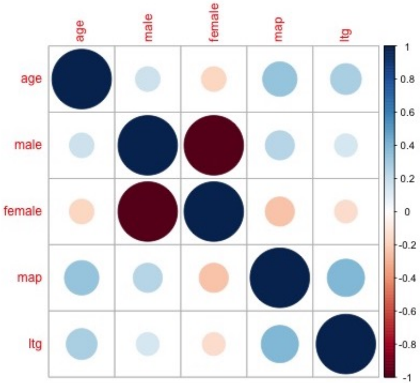
- Note the following correlation matrix captures the correlation between the samples and is of dimension $n \times n$

$$c\hat{o}r(x^t) = \frac{1}{p-1}\underbrace{x_s}_{n\times p}\underbrace{x_s^t}_{p\times n}$$

Correlation matrix

R commands

- `cov()` sample covariance matrix
- `cor()` sample correlation matrix
- `corrplot()` to visualise



The rank of a matrix

- Consider a matrix x of dimension $n \times p$.

$$\underbrace{x}_{n \times p}$$

- The rank of matrix x is the minimum of n and p.
- If we have more samples than variables $(n > p)$ the rank is p.
- If we have less samples than variables $(n < p)$ the rank is n.

The rank of the correlation matrix

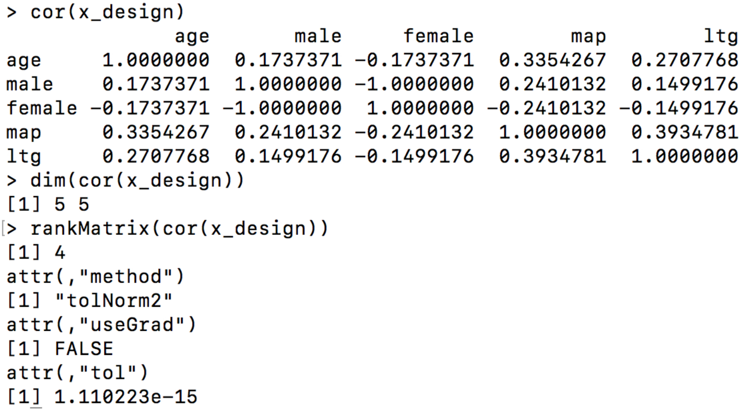
- Let us consider again the correlation matrix

$$\hat{cor}(x) = \frac{1}{n-1} \underbrace{x_s^t}_{p \times n} \underbrace{x_s}_{n \times p}$$

- The theoretical rank of the correlation matrix is the minimum of n and p.
- To test the rank of a matrix in R: `rankMatrix()` in the `Matrix` package

If the rank of a correlation matrix is smaller than $min(n, p)$ the correlation matrix is singular and thus cannot be inverted.

The rank of the correlation matrix in R



```
> cor(x_design)
              age       male     female        map        ltg
age     1.0000000  0.1737371 -0.1737371  0.3354267  0.2707768
male    0.1737371  1.0000000 -1.0000000  0.2410132  0.1499176
female -0.1737371 -1.0000000  1.0000000 -0.2410132 -0.1499176
map     0.3354267  0.2410132 -0.2410132  1.0000000  0.3934781
ltg     0.2707768  0.1499176 -0.1499176  0.3934781  1.0000000
> dim(cor(x_design))
[1] 5 5
> rankMatrix(cor(x_design))
[1] 4
attr(,"method")
[1] "tolNorm2"
attr(,"useGrad")
[1] FALSE
attr(,"tol")
[1] 1.110223e-15
```

- Interpretation: The correlation matrix of the design matrix with 5 predictors is of dimension 5 × 5, yet the rank is 4 which indicates singularity.

Outlook: Big data ($n << p$)

- Assume we are considering a big data set with much more variables than observations $n << p$

$$\hat{cor}(x) = \frac{1}{n-1} \underbrace{x_s^t}_{p \times n} \underbrace{x_s}_{n \times p}$$

- The theoretical rank of the correlation matrix is the minimum of n and p ($min(n, p)$).
- In case of big data, the rank of the matrix is n, which is much smaller than p.
- Thus the correlation matrix (and also $x_s^t x_s$) are singular and cannot be inverted.
- It is not possible to compute the ordinary least squares estimate for big data.

Variance inflation factor (VIF)

- The VIF is the ratio of the variance of β_j when fitting the full model divided by the variance of $\beta_{UNI}(j)$ in a unvariable linear model.
- Lowest possible value is 1 (no collinearity).
- Rule of thumb: If VIF > 10, this indicates strong multicollinearity, but already smaller VIF can impact the analysis.
- It provides an indication how much the variance of an estimated regression coefficient is increased because of multicollinearity.

Variance inflation factor (VIF)

Consider the following linear model including p predictors with inde $j \in 1, ..., p$

$$y = \alpha + \beta_1 x_1 + \beta_2 x_2 + ... + \beta_j x_j + ... + \beta_p x_p + \epsilon.$$

1. For the first variable $j = 1$ fit a linear model, where x_1 is the outcome and all other variables x_{-1} are the predictors

$$x_1 = \alpha + \beta_2 x_2 + ... + \beta_j x_j + ... + \beta_p x_p + \epsilon.$$

2. Estimate $R_2(1)$, the proportion of variance of x_1 explained by the other predictors x_{-1}.
3. The VIF for variable 1 is defined as

$$VIF_1 = \frac{1}{1 - R_2(1)}$$

4. Repeat for the other $j \in 2, ..., p$.

Variance inflation factor

R commands

- `vif()` in the *R*-package `car`
- Computes variance-inflation and generalized variance-inflation factors for linear and generalized linear models.

```
> lm2=lm(y~age+male+map+ltg, data=x)
> vif(lm2)
     age     male      map      ltg
1.166584 1.075047 1.306446 1.216982
```

- Interpretation: No variable has a VIF > 10, with around 1 they are rather low and there is no indication of multicollinearity.

Singular value decomposition and condition number

Singular value decomposition of a matrix m (dimension $n \times p$) is defined as

$$m = u\Sigma v$$

- Σ: Matrix of singular values (dimension $n \times p$)
- u: Left-singular vectors (dimension $n \times n$)
- v: Right-singular vectors (dimension $p \times p$)

Singular value decomposition and condition number

- A singular value decomposition of the sample correlation matrix produces p singular values d_1 to d_p.
- After sorting the eigenvalues in decreasing order

$$d_{[1]} > ... > d_{[j]} > ... > d_{[p]}$$

  - ◇ $d_{[1]}$ is the largest singular value
  - ◇ $d_{[p]}$ is the smallest singular value

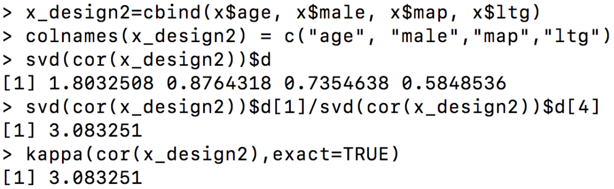
Condition number

Ratio of largest over smallest singular value.

$$\kappa = d_{[1]}/d_{[p]}$$

Singular value decomposition in R

- Singular value decomposition: `svd()`
  Value $*d*$ extracts the singular values
- Condition number: `kappa()`
  Use argument `exact=TRUE`



```
> x_design2=cbind(x$age, x$male, x$map, x$ltg)
> colnames(x_design2) = c("age", "male","map","ltg")
> svd(cor(x_design2))$d
[1] 1.8032508 0.8764318 0.7354638 0.5848536
> svd(cor(x_design2))$d[1]/svd(cor(x_design2))$d[4]
[1] 3.083251
> kappa(cor(x_design2),exact=TRUE)
[1] 3.083251
```

- Interpretation: The condition number is far below 30, which is often used as a rule of thumb. There is no sign of multicollinearity.

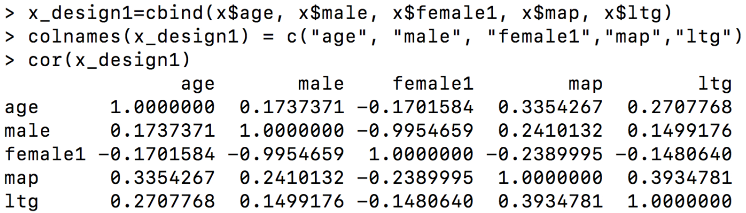
Example: Diabetes data

- age: age of the subject
- male: binary indicator if male
- female1: binary indicator if female, but one sample is wrongly annotated

→ cor(male,female1) = -0.9954659

- map: blood pressure
- ltg: triglycerides

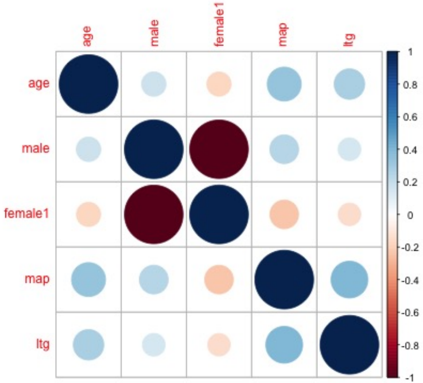
Correlation matrix



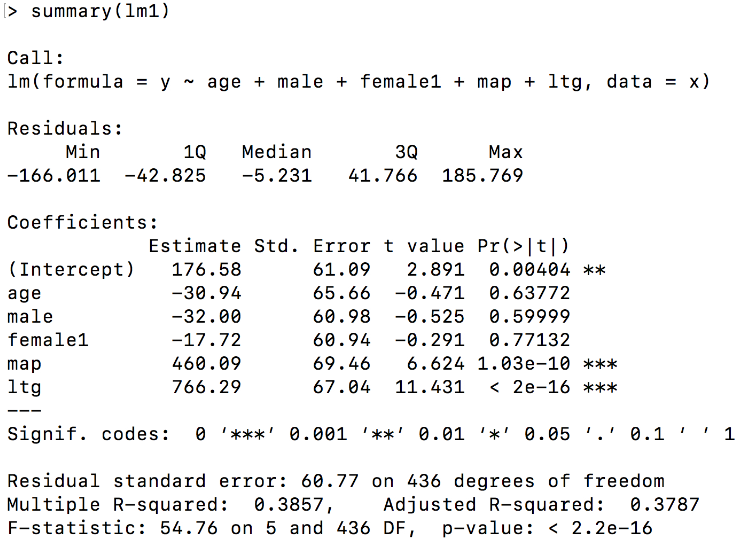
```
> x_design1=cbind(x$age, x$male, x$female1, x$map, x$ltg)
> colnames(x_design1) = c("age", "male", "female1","map","ltg")
> cor(x_design1)
               age       male    female1        map        ltg
age      1.0000000  0.1737371 -0.1701584  0.3354267  0.2707768
male     0.1737371  1.0000000 -0.9954659  0.2410132  0.1499176
female1 -0.1701584 -0.9954659  1.0000000 -0.2389995 -0.1480640
map      0.3354267  0.2410132 -0.2389995  1.0000000  0.3934781
ltg      0.2707768  0.1499176 -0.1480640  0.3934781  1.0000000
```

Example: Diabetes data

Correlation matrix corrplot



Example: Diabetes data



```
> summary(lm1)

Call:
lm(formula = y ~ age + male + female1 + map + ltg, data = x)

Residuals:
     Min       1Q   Median       3Q      Max 
-166.011  -42.825   -5.231   41.766  185.769 

Coefficients:
            Estimate Std. Error t value Pr(>|t|)    
(Intercept)   176.58      61.09   2.891  0.00404 ** 
age           -30.94      65.66  -0.471  0.63772    
male          -32.00      60.98  -0.525  0.59999    
female1       -17.72      60.94  -0.291  0.77132    
map           460.09      69.46   6.624 1.03e-10 ***
ltg           766.29      67.04  11.431  < 2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Residual standard error: 60.77 on 436 degrees of freedom
Multiple R-squared:  0.3857,	Adjusted R-squared:  0.3787 
F-statistic: 54.76 on 5 and 436 DF,  p-value: < 2.2e-16
```

Example: Diabetes data

- The linear model can be calculated now since there is no exact collinearity.
- Note that male and female have both a negative regression coefficient.
- VIF()

```
> lm1=lm(y~age+male+female1+map+ltg, data=x)
> vif(lm1)
      age        male     female1         map         ltg
 1.167432 110.819281 110.626114    1.306447    1.217015
```

- Interpretation: VIF for male and female1 is highly inflated and indicates strong multicollinearity.
- This inflation distorts the linear model and hinders the interpretation of the male and female1 regression coefficients.

Example: Diabetes data

- Singular value decomposition and condition number

```
> x_design2=cbind(x$age, x$male, x$female1, x$map, x$ltg)
> colnames(x_design2) = c("age", "male","female1","map","ltg")
> svd(cor(x_design2))$d
[1] 2.323503750 1.346325644 0.736162810 0.589481033 0.004526764
> svd(cor(x_design2))$d[1]/svd(cor(x_design2))$d[5]
[1] 513.2814
> kappa(cor(x_design2),exact=TRUE)
[1] 513.2814
```

- Interpretation: The condition number is very high ($>>30$) and indicates strong multicollinearity.

How to prevent multicollinearity?

- Grouping
- Partial least squares
- Pre-whitening

Grouping

- When there is biological knowledge of pre-defined groups of variables (e.g. genes within a pathways, lipid characteristics of specific subfractions), it is advised to group them and use only one variable within the group as representative.
- Group structures can be defined using unsupervised learning approaches such as clustering.
- Projections into a lower-dimensional space
  - Principle component analysis (PCA)
  - Independent component analysis
  - Non-negative matrix factorisation

Partial least squares

- PLS is a dimension reduction approach that is coupled with a regression model.
  1. Create latent components t as a linear transformation of x (dimension $n \times p$)
  2. Create latent components u as a linear transformation of y (dimension $n \times k$)

$$\underbrace{x}_{n\times p} = \underbrace{t}_{n\times l}\underbrace{q_x^t}_{l\times p} + \epsilon_x$$

$$\underbrace{y}_{n\times k} = \underbrace{u}_{n\times l}\underbrace{q_y^t}_{l\times k} + \epsilon_y$$

  3. Idea: The latent components have a smaller dimension $l < p$.
  4. Aim: Find decompositions of both x and y that maximise the covariance between the latent components t and u.
- R-package: `pls`

Pre-whitening

- Prewhitening transformations are matrix operations that ‘remove’ correlation.
- Suppose x has a mean vector of 0 and covariance matrix Σ.
- There exists a whitening matrix w that satisfies $w^t w = \Sigma^{-1}$.
- The prewhitened data $x^\star$ is defined as

  $$x^\star = wx,$$

  where the covariance of $x^\star$ is diagonal.
- There are several algorithms to compute w
  - Mahalanobis transformation $w = \Sigma^{-1/2}$
  - Cholesky decomposition of Σ
  - PCA based
- R-package: `whitening`

Take away: Variable selection with correlated predictors

- Exact correlation between predictors can cause singularity of the correlation and covariance matrix.
- Strong correlation between predictors can cause multicollinearity.
- Multicollinearity can distort linear regression models and inflate the variance of the estimate.
- How to detect singularity?
  - Rank of the between predictor correlation matrix
- How to detect multicollinearity?
  - Variance inflation factor
  - Condition number based on the ratio of largest over smallest singular value